

Pathology is the study of disease producing constellations and their effect on living organisms. It has reared itself since the time of Virchow to the status of a science, if any field in biology may be truly called a science, and as such has and can divorce itself from its previous servile position as the hand maid of medicine.; yet , for us its greatest *raison d'être* is the part it plays in elucidating the processes of disease in man. It is well to remember from the very beginning however that the purpose of any science is to reconstruct physical experience into a system of law and order,; to bring natural phenomena closer to our comprehension.

The domain of science is one of "causal explanations". Purpose , as such, lies outside of this realm, teleology must find its proper scope elsewhere. The moon was not hung aloft in the heavens to keep our gas bills down, neither does blood clot to prevent a man from bleeding to death. The formation of the clot may be the saving factor, but its formation^{tion} is the result of a definite series of genetically related processes or steps, the absence of any one of which precludes the possibility of success, the presence of them all is tantamount to its completion. So again, bacteria , per se, are not the cause of disease, but rather are they but a single link in a long concatenation of causally connected events which include such other links as hereditary background, environment, age, sex, mental attitude , previous state of health and the variable factors such as type, morphology, mass, and virulence of the bacteria themselves.

What is disease? It may be considered as the reflection of a pathological process or lesion upon the organism as a whole. What is a pathological lesion? It may be defined as a morphological expression of disproportion of values between stimuli and living cells. All living processes may be considered as a resultant of the interplay between various stimuli and the response of living tissue to these stimuli. If the stimulation is of short duration and of mild intensity and the activated tissue returns quickly to a state of equilibrium, - then the process may be considered as physiological.

If on the other hand the stimuli are of great intensity and prolonged in time, then the result may usually be considered as pathological. To state this in another way - irritants are environmental factors which are responsible for the emancipation of organismic potentialities. The degree of disproportion between the stimulating effect of an irritant and the response on the part of the organism determines physiology or pathology. A cloth dipped in water heated to 55°C and applied to a part causes a physiological increase in activity of a part with a pleasing effect and a rapid return to its previous state when the mild irritant is removed. Increase the temperature of the water to 100°C and it stimulates just a bit too much, and on removal there is no rapid return to the status quo ante because actual damage has been done to the tissue and this "burn" is pathological.

As beginning pathologists let us take a part of our early guidance from that great pathologist, Virchow, who said many years ago:

(1) All knowledge of disease must be based upon objective, anatomical experience.

(2) Conclusions as to the nature of disease must be based on this experience and be made strictly according to natural laws of cause and effect."

There may be many exceptions to these rules at the present time but they still may serve as a sure foundation for accurate, restrained, scientific thinking in pathology. At times, perchance we shall leave our special field and indulge in theorizing and interpretation and where facts fail us take the perfectly legitimate heuristic, somewhat circuitous route to truth, but when so doing we knowingly leave the sphere of pure science and enter the domain of philosophy and metaphysics.

With these few introductory remarks let us begin our work with a consideration of some of the changes that take place in tissues.

Jan. 7, 1936

Progreessive Movements

Morphological Fluidity

The basic factor in growth; characteristic of higher forms; antedates birth, postdates death.

Differentiation - a function of environment

1. Mitotic - at rest
2. Amitotic - inactive cells

Growth Requisites

1. Transudation - increased nutritive supply
2. Assimilation - ability of the tissue to use it; depends on the permeability of the cell
3. Procreation - formation of new protoplasm

Protomeres

Smallest living units which have all of the characteristics of living protoplasm. These increase in geometrical progression from generation, the nuclear plasma material, however, remaining in constant proportion.

Cloudy Swelling

When on the positive side it is the first step in the process of greater assimilation and increase in protoplasmic content.

Hypertrophy

Increase in protoplasmic content and structures already present

Hyperplasia

Numerical increase in cell elements and protoplasmic content. Both content and function are constant in type

Regeneration

An inherent characteristic of living matter. Young cells form an ANLAGEN whose direction of differentiation is then a function of environment. There is always a tendency to overproduce.

Connective Tissue - from fibroblasts

Cartilage - from perichondroblasts or fibroblasts

Bone - from periosteum, endosteum or chondroclasts(?)

Vessels - endothelial buds from preexisting vessels

Blood - reappearance of myeloid foci of embryonic type in bone marrow, liver and spleen

Muscles - hypertrophy rather than hyperplasia the rule

Neuroglia - from new formed astrocytes

Nerve - by extension from the proximal part of the fiber only

Ganglion Cell - no true regeneration when totally destroyed

Epithelial Cells

Lining - Parenchymal - no true regeneration if integrity of the architectural plan has been disturbed

Abnormal Regeneration

Abortive or pathological, the result of destruction of normal skeletal structure by trauma or disease

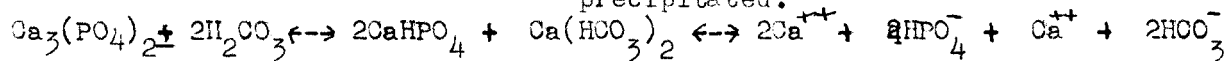
Scar Tissue - substitution of lower tissue in injury

Calcium

Normal - 10 mgrms. % in blood, maintained by the activity of the parathyroid glands

Two types

1. Indeffusible - firmly bound in such tissues as the bones
2. Diffusible
 - a. Unionized - playing very little part in the active metabolism of the body
 - b. Ionized - the amount in ionic form depends on the carbonic acid tension; when it is reduced the equation goes from left to right and the insoluble tricalcium phosphate is re-precipitated.



Function

1. Blood Clotting
 - Prothrombin - Cephalin - Ca -- Thrombin
 - Thrombin - Fibrinogen -- Fibrin
2. Increases contraction of heart muscle
3. Direct relation ship to nervous irritability
4. Formation of bones
5. Balance in Hydrogen ion maintainance

Causes of Increase in Calcium

1. Haliteresis - withdrawal of Ca. from bones as seen in osteomalacia. Calcification follows in the acid juices of such tissues as the stomach and kidney in the presence of alkaline tissue juices
2. Parathyroid underactivity - in case of tumor displacement of a great deal of the tissue
3. Paget's Disease of Bones - classification rather obscure at the moment but there is increase in Ca.
4. Hyperostosis Frontalis Interna - Surg., Gyn., & Obs. 61-353-35

Decrease in Calcium

1. Parathyroid over activity
2. Alkalaemia
 - a. Gastrointestinal - loss of HCl by vomiting
 - b. Hyperpnoea - blowing off of CO₂
 - c. Alkalie ingestion - excess NaOH
3. Rickets - in complete absorption from G. I. tract
4. Nephritis - incomplete riddance ?

Calcification

1. Always in degenerated, necrotic, hyaline tissue such as arterial walls in hypertension, atherosclerotic plaques, avascular tumors, scar tissue, abscesses, Tbc. nodes, & exudates, cysts, incrustated parasites etc.

Why Calcification ?

1. Physical deposition theory
2. Fatty acids form insoluble soaps
3. Supersaturation maintained by high CO₂ tension
4. Necrosis and hyaline metamorphosis 2

Why in bone at all?

Growing bone contains an enzyme capable of splitting hexose phosphate into hexose & inorganic phosphate.

Concretions

- A. Nephrolithiasis
- B. Cholelithiasis
- C. Pancreatic lithiasis

(9)

vascular tumors, scar tissue, abscesses,
the nodes & nodules, cysts, parasites (Trichinella)

Why calcification

- (1) Physical deposition
- (2) Fatty acids to form soaps.
- (3) Super saturation maintained by high CO_2 tension
- (4) Necrosis & hyaline metamorphosis

Why calcification in bone at all

Growing bone contains an enzyme capable
of splitting hexose phosphate into hexose & inorganic phosphate ppt. $\text{Ca}_3(\text{PO}_4)_2$ 85% bone.

Concretions -

(1) Kidney Stones - Nephrolithiasis
J. A. M. A. 104 #15 - 1299 April 1935
D. K. Kuyser & Swift J. Lab. J. Med. 32: 541-34

Experimental production (see cond 1)

- (1) Oxalates
- (2) Excessive CaOx diet
- (3) Parathyroid or parathyroid extract
- (4) Uric acid crystals in animals & E. coli fistulas
- (5) Vitamin A deficiency
- (6) Infection & urea splitting strep staph & B. Proteus
- (7) Incubation in presence of infection

(10)

Types	Ca PO_4	Ca CO_3	Amino Acid.
	Vitamins & etc	Alkalies & acids	Acids.

(2) Gall Bladder

- (1) Cholesterol - pure
- (2) Pigment - - pure
- (3) Infection -
- (4) Mixed.

Theories: Werner Horay . Arch Path 17-1-34

- (1) Aschoff 1924 - High blood cholesterol, + stones
- (2) Conrained 1933 - Walther - blood-like cholesterol.
- (3) Nanniger - 1892 - disintegration of epithelium of GB
- (4) Elnam + Graham 1932 - support Nanniger. to account for crystals in stony gallbladder.

Schade:- The increasing impoverishment of the bile in cholate content compels small quantities of cholesterol to settle out. But owing to the presence of fat it is guttulate separation which occurs, and since in such simple stasis foreign substances are lacking, there is nothing to prevent aggregation of the droplets. (A. Schade Colloid Chemistry 1/4. 1928-2, 503)

Inadequate.

(11)

The following states the anat. or phys. abnormalities the bile collects. During this period there may be infiltration of cholesterol from hypercholesterolemia blood and a decrease in the amount of the alkali cholates which are responsible for emulsifying. The effect is in the form of an emulsion as well as the cholesterol in the dispersed state. In the absence of infection, a decrease in cholates may result from either or both of the following causes

(1) A change in the pH of the bile from alkaline to the acid, converting the alkali salt to the insoluble glycocholic acid which is neither an emulsifying agent for fat nor a peptizing agent for cholesterol (or)

(2) A physiologic change in the wall of the gall bladder which allows resorption of the alkali cholates.

The disappearance of alkali cholate, either by conversion to glycocholic acid or by resorption causes ppt of cholesterol. The excess cholesterol collects around the fat droplets which tend to coalesce as the cholate is gradually removed, then the fat acts as a solvent which is responsible for the growth of interlacing crystals.